REMARKS

Claims 1-34 are pending. No claim amendments are made herein.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. (Office Action, page 2)

The applicants respectfully disagree that the filtration step is considered new matter as it is supported in the specification in the paragraphs below among other places (emphasis added):

> [0047] When a hydrophobic membrane is used as the solid-phase, for example, a method of dropping the immobilization sample onto the hydrophobic membrane and allowing the immobilization sample to sink into the hydrophobic membrane by standing, a method of conventional filtration method, where ***the immobilization sample is filtered by suction through the hydrophobic membrane,*** or a centrifugal filtration method, etc. may be used.
>
> [0048] The method for ***immobilizing a protein by the filtration method will be explained specifically*** by mentioning the method using a commercially available dot blotter or a slot blotter as follows.

The assertion, "Indeed, different permutations of the term, e.g. filtrate, filtration, are not disclosed in the specification," (Office Action p.2, second paragraph) is deemed rebutted by the specification disclosure which provides literal support for these terms and thus the rejection is deemed overcome.

Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishibu et al., Analytical Biochemistry (2003) 319:88-95 ("Nishibu"). (Office Action, page 3)

The 35 USC § 102(b) rejection is moot because the effective filing date of the instant application is the date of the original PCT application, namely PCT/JP2004/000504 which has a filing date of January 21, 2004, which is within a year of Nishibu's disclosure date of August 1, 2003. *Broadcast Innovation, L.L.C. v. Charter Communs., Inc.*, 420 F.3d 1364, 76 U.S.P.Q.2d 1220 (Fed. Cir. 2005) (A reversal of the district court's error in not giving a patent the benefit of the filing date of the original PCT application).

Explaining that effective filing date of a 35 USC § 371 national stage application is the same date as the original PCT application, the Federal Circuit stated in *Broadcast Innovation, L.L.C. v. Charter Communs., Inc.*, 420 F.3d 1364, 1368, 1369 (Fed. Cir. 2005):

> As previously mentioned, the applicant filed the '595 patent on July 18, 1995, as the U.S. national stage application of the original PCT application. However, July 18, 1995 is not the "U.S. filing date" of the '595 patent. Specifically, under 35 U.S.C. § 363, ***the international filing date of a PCT application is also the U.S. filing date for the corresponding national stage application***. 35 U.S.C. § 363 (1984); see also Manual of Patent Examining Procedure (MPEP) § 1893.03(b) (8th Ed. including May 2004 revisions) ("It should be borne in mind that the filing date of the international application is also the filing date for the national stage application."). Thus, the '595 patent's U.S. filing date is November 26, 1993, the filing date of the PCT application. Because the '094 patent is entitled to priority back to the '595 patent's U.S. filing date, the '094 patent's priority date under 35 U.S.C. § 120 as well as its term calculation date under 35 U.S.C. § 154(a)(2) is at least November 26, 1993. ***In other words, the '094 patent, which specifically references the '595 patent and thus satisfies the requirements of 35 U.S.C. § 120 and 37 C.F.R. § 1.78(a), is entitled to effectively the same date as the original PCT application.*** (emphasis added)

Therefore, applying the holding of *Broadcast Innovation* here, Nishibu is removed as a reference under 35 USC § 102(b) because the Nishibu publication date is not more than one year before the instant application's filing date, making this rejection moot.

Claims 1-5 and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheley et al., Biotechniques (1991) 10(6):731-732 ("Cheley"), cited in the IDS filed July 22, 2008, in view of Jacobson, Electrophoresis (1990) 11:46-52, cited in the IDS filed July 13, 2006. (Office Action, page 5)

The Applicant asserts that because ***Jacobson indicates that SDS is not preferable for binding in nitrocellulose, the skilled artisan would not have motivation to modify Cheley's method with Jacobson.*** In the Response to Arguments on p.11-12 of the Office Action, it is alleged:

> Jacobson, however, is relied upon in part to teach a PVDF membrane. The combination of Cheley and Jacobson would therefore have PVDF, not nitrocellulose, as the immobilizing membrane. Although PVDF and nitrocellulose are equivalent materials for the same function, Jacobson does not indicate that PVDF in the presence of SDS would cause a decrease in binding like nitrocellulose does. Moreover, Jacobson describes PVDF as a membrane with good mechanical strength and that using methanol would increase binding…Accordingly, even if SDS did reduce binding with a PVDF membrane, the methanol would provide a counter to this decrease and the PVDF's mechanical qualities provide an incentive for using it as a protein substrate. One of ordinary skill in the art would therefore still have a reason to combine Jacobson with Cheley's method. (Office action p.11, line 14 to p.12, line 5).

The Applicant respectfully disagrees. Jacobson describes that PVDF and nitrocellulose are equivalent materials for the same function. Jacobson in fact indicates that it is preferable to bind protein to ***nitrocellulose membrane in the presence of methanol*** (P.47, left column, 3.1 Buffer composition, lines 4 to 6, p.48, Fig. 1). Therefore, the skilled artisan would logically understand from the disclosure that it is preferable to bind protein to ***PVDF membrane in the presence of methanol***.

In contrast, Jacobson indicates that ***the binding (of protein) to nitrocellulose was lower in the presence of SDS*** (p.47, right column, lines 17 to 18, Fig.2b, p.49, right column lines 16 to 17,"SDS reduces the binding to nitrocellulose."). Therefore, while Jacobson does not indicate that PVDF membrane in the presence of SDS would cause a decrease in binding like nitrocellulose does, the skilled artisan would nonetheless understand from Jacobson that ***the binding of protein to PVDF membrane is lower in the presence of SDS, as well.*** Therefore, the skilled artisan would logically conclude that ***it is not preferable to bind protein to PVDF membrane in the presence of SDS***.

Jacobson does not disclose the binding of protein to PVDF membrane ***in the presence of methanol and SDS***. On the other hand, Jacobson indicates that

> ...presumably by strengthening the hydrophobic interactions between protein and membrane and by ***weakening the binding of SDS to protein*** (p.49, right column,

line 7 to 10).

Again, the rejection alleges that:

> ...even if SDS did reduce binding with a PVDF membrane, the methanol would provide a counter to this decrease and the PVDF's mechanical qualities provide an incentive for using it as a protein substrate. The skilled artisan would therefore still have a reason to combine Jacobson with Cheley's method. (Office action, p.12, lines 1 to 5).

The skilled artisan would not logically understand to perform protein binding to PVDF membrane in the presence of SDS ***because the artisan knows that SDS reduces the binding of protein to nitrocellulose membrane*** from the disclosure of Jacobson, as alleged. Further, Jacobson does not indicate whether protein can be bound to nitrocellulose membrane as well (or better) in the presence of methanol and SDS, as in the presence of methanol only. Therefore, the assertion that "even if SDS did reduce binding with a PVDF membrane, the methanol would provide a counter to this decrease" has no logical basis in the art cited in the rejection.

As is clear from the instant specification:

> [0034] Generally, surfactants such as nonionic surfactant have a property to inhibit adsorption of a hydrophobic substance. On the contrary, binding of a protein to a membrane is thought to occur by hydrophobic bonding. For this reason, surfactants have not been preferably used in the immobilization of proteins. Consequently, there are few reports discussing on an action of a surfactant against a protein and an interaction between the protein receiving the action and a solid-phase surface in detail. For this reason, it has not been known until now that a long chain alkyl sulfate as a kind of surfactant is effective for immobilization of a protein.

Thus, the skilled artisan would perform binding of protein in the presence of methanol only, but would not think to add SDS, because of the disclosures in the cited art.

Based on the rebuttal above, there is in fact no logical motivation to combine Cheley and Jacobson, and thus the combination of Jacobson with Cheley's method is impermissible

hindsight.

Additionally, a protein in a sample in the presence of a surfactant cannot be immobilized efficiently by the conventional immobilization method as explained in [0015].

In contrast to this, by using the claimed invention, proteins can be immobilized to the solid-phase having hydrophobic surface in the presence of a lower alcohol, and a halogenocarboxylic acid and/or a long chain alkyl sulfate ***at a constant rate, even in the presence of SDS***, which is unexpected based on the cited art.

As explained in the present specification (emphasis added),

> [0155] … A rate of variability between the points means a value, in which the change of signal intensity accompanied to the change of SDS concentration is calculated as a rate of variability. It is indicated that as number of the value becomes smaller, signal intensity (result of measurement) becomes more stable without being influenced by the SDS concentration.
>
> [0159] From the above facts, since the rate of variability between points can be stabilized at a SDS concentration not less than 0.1% (W/V), it is understood that when a protein is immobilized by using the immobilizing reagent solution containing SDS within such concentration range, quantitative determination of the protein in the sample can be achieved exactly.
>
> [0206] ***As is clear from Table 3***, when the protein is measured by the solid-phase method of the present invention, the measurement results within .+-.20% to the control can be obtained in almost all proteins even in the sample containing 2% (W/V) SDS, and ***it is understood that detrimental effect of SDS in the protein sample on the determination of protein can be avoided***.
>
> [0207] Contrary, when the measurement is performed with the liquid-phase method using the sample containing ***2% (W/V) SDS, the measurement could not be achieved at all.***
>
> [0208] From the above results, it is understood that the method for immobilizing

a protein and the method for quantitative determination of protein of the present invention can be applied to all proteins. Also, ***the method became clear to be further more useful on the point that the quantitative determination of a protein in a sample containing a known inhibitor for determining protein, especially SDS which is widely used as a solubilizing agent for protein.***

[0232] Accordingly, it is understood that the immobilization method of a protein of the present invention can solve the problem caused by a surfactant that is widely used as a conventional additive, that is, the problem of inhibition of the quantitative determination of a protein.

In light of these unexpected results, which are clearly not disclosed or suggested by the cited art, as explained above, the claimed invention is not *prima facie* obvious over the combination of Cheley and Jacobson. The claimed invention simply has an unexpected superior effect which the cited art teaches against.

It is respectfully requested that the rejection be reconsidered and withdrawn.

Claims 6-7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheley in view of Jacobson, as applied to claim 1. (Office Action, page 8)

For the same reasons explained above, there is no motivation to combine Jacobson with Cheley, and the claimed invention has the above-described unexpected superior effect to the disclosure of Cheley and Jacobson.

It is respectfully requested that this rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105.

Dated: October 7, 2009

Respectfully submitted,

Customer No. 21874

Electronic signature: /James E. Armstrong, IV/
James E. Armstrong, IV
Registration No.: 42,266
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(202) 478-7375
Attorneys/Agents For Applicant